ATENT T

Attorney Docket No.: 015389-002630US Client Reference No.:018/212C

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Thomas R. Cech et al.

Application No.: To Be Assigned

Filed: Herewith

For: HUMAN TELOMERASE CATALYTIC SUBUNIT: DIAGNOSTIC AND THERAPEUTIC METHODS Examiner:

To Be Assigned

Art Unit:

To Be Assigned

INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR §1.97 and

§1.98

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. In accordance with 37 CFR §1.98(d), copies of the references can be found in Application No. 08/912,951, filed August 14, 1997 (Attorney Docket No. 015389-002600US). If the examiner would like additional copies of any of these cited references, applicants will happily provide them.

It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom. As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

Applicant believes that <u>no fee is required</u> for submission of this statement, since it is being submitted prior to the first Office Action. However, if a fee is required, the



Thomas R. Cech et al. Application No.: To Be Assigned Page 2

Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,

Hugh Wang Reg. No. 47,163

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Tel: 650-326-2400 Fax: 650-326-2422

HW:adm

PA 3194170 v1

Substitute for form 1449A/PTO

PTO/SB/08A (08-00) Approved for use through 10/31/2002. OMB 0651-0031

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Application Number	To Be Assigned			
Filing Date	Herewith	7-		
First Named Inventor	Cech, Thomas J.			
Group Art Unit	To Be Assigned	W.		
Examiner Name	To Be Assigned	55		
Attorney Docket Number	015389-002630US	45		
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				U.S. PATENT DOCUM	MENTS	
Examiner Initials *	Cite No. ¹	U.S. Patent Doo Number Kind (if kno	Code ²	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A	08/751,189		Harrington, et al.	11/15/96	. igaroo rippoui
	В	60/038,750		Counter, et al.	02/20/97	· · · · · · · · · · · · · · · · · · ·
	С	3,817,837		Tanenholtz et al.	06-18-74	
	D	3,850,752		Schuurs et al.	11-26-74	
	Ε	3,939,350		Kronick et al.	02-17-76	
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		4,366,241		Tom et al.	12-28-82	
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	K	4,683,202		Mullis	07-28-87	
	L	4,816,567		Cabilly et al.	03-28-89	
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	N	5,489,508		West et al.	02-06-96	
	0	5,583,016		Villeponteau et al.	12-10-96	
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	Q	5,770,422		Collins	06-23-98	
	R	6,093,809		Cech, et al.	07/25/00	
	S	6,258,535	B1	Villeponteau et al.	07/10/01	
	Т	6,261,556	B1	Weinrich et al.	07/17/01	
	J	6,261,836	B1	Cech et al.	07/17/01	

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Examiner Initials*	Cite No. ¹	Office ³	Number	id Code ⁵ known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Where Relevant Passages or Relevant Figures Appear	T ⁶	
	V	JP	09154575-A			06-17-97			
	W	PCT	WO 84/03564			09-13-84			
	Х	PCT	WO 95/13382			05-18-95			
	Υ	PCT	WO 96/01835		****	01-25-96			
	Z	PCT	WO 96/12811			05-02-96			
	AA	PCT	WO 96/19580			06-27-96			

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				Application Number	To Be Assigned	
INFO	DRMATION	DIS	CLOSURE	Filing Date	Herewith	
STA	STATEMENT BY APPLICANT		First Named Inventor	Cech, Thomas J.		
				Group Art Unit	To Be Assigned	
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Sheet	2	of	10	Attorney Docket Number	015389-002630US	

	FOREIGN PATENT DOCUMENTS								
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Examiner Initials*	Cite No. ¹	Office ³	Number ⁴ Kind Code ⁵ (<i>if known</i>)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Where Relevant Passages or Relevant Figures Appear	T ⁶		
	AB	PCT	WO 96/40868		12-19-96				
	AC	PCT	WO 98/01542		01-15-98	•			
	AD	PCT	WO 98/01543		01-15-98				
	AE	PCT	WO 98/07838		03-05-98	.,			
	AF	PCT	WO 98/08938		02-26-98				
	AG	PCT	WO 98/21343		05-22-98				
	AH	PCT	WO 98/37181		08-27-98				
	Al	PCT	WO 98/45450		10-15-98	h			
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	AK	PCT	WO99/01560		01/14/99				

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INFORMATION DISCLOSURE	Filing Date	Herewith		
STATEMENT BY APPLICANT	First Named Inventor	Cech, Thomas J.		
	Group Art Unit	To Be Assigned		
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Sheet 3 of 10	Attorney Docket Number	015389-002630US		

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	_
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Т
	AL	1994 Genome Issue of Science (265:1981f)	
	АМ	Anderson and Young, "Quantitative Filter Hybridization" in <i>Nucleic Acid Hybridization</i> pp73-111 (1985)	
	AN	Ausubel et al., Current Protocols in Molecular Biology, John Wiley & Sons, New York NY (1989)	
	AO	Autexier et al., "Reconstitution of human telomerase activity and identification of a minimal functional region of the human telomerase RNA," (1996) EMBO J, 15:5928	
	AP	Auxexier and Greider, "Functional reconstitution of wild-type and mutant <i>Tetrahymena</i> telomerase," (1994) <i>Genes Develop.</i> , 8:563	
	AQ	Berger and Kimmel, Guide to Molecular Cloning Techniques, Meth. Enzymol., vol. 152, Academic Press, San Diego CA (1987)	
	AR	Biessman et al., "Addition of Telomere-Associated HeT DNA Sequences "Heals" Broken Chromosome End s in Drosophila," (1990) Cell, 61:663	
	AS	Bitter et al., "Expression and secretion vectors for yeast," Meth Enzymol., (1987) 153:516	
	AT	Blackburn and Chiou, "Non-nucleosomal packaging of a tandemly repeated DNA sequence at termini of extrachromosomal DNA coding for rRNA in Tetrahymena," (1981) <i>Proc. Natl. Acad. Sci.</i> , 78:2263	
	AU	Blackburn and Gall, " A tandemly repeated sequence at the termini of the extrachromosomal ribosomal RNA genes in <i>Tetrahymena</i> , " (1978) <i>J. Mol. Biol.</i> , 120:33	
	AV	Blackburn, "Telomerases," (1992) Ann. Rev. Biochem., 61:113	
	AW	Bodnar et al., "Extension of Life-Span by Introduction of Telomerase into Normal Human Cells," (1998) Science, 279:349	
	AX	Bradford, "A Rapid and Sensitive method for the Quantitation of Microgram Quantities of Protein Utilizing the Principle of Protein-Dye Binding," (1976) Anal. Biochem., 72:248	
	AY	Braunstein et al., "Transcriptional silencing in yeast is associated with reduced nucleosome acetylation," (1993) Genes Develop., 7:592	

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•		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	AZ	Calvio et al., "Identification of hnRNP P2 as TLS/FUS using electrospray mass spectrometry," (1995) RNA, 1:724	
	ВА	Caruthers et al., "New chemical methods for synthesizing polynucleotides," (1980) Nucleic Acids Res. Symp. Ser., 215-223	
	ВВ	Chan and Tye, "Organization of DNA sequences and replication origins at yeat telomeres, " (1983) Cell, 33:563	
	вс	Colbere-Garapin et al., "A new dominat hybrid selective marker for higher eukaryotic cells," (1981) J. Mol. Biol., 150:1	
	BD	Cole et al., "The EBV-hybridoma technique and its application to human lung cancer," Monoclonal Antibodies and Cancer Therapy, Alan R. Liss Inc., New York NY 77-96 (1985)	
	BE	Collins et al., "Purification of Tetrahymena telomerase and cloning of genes encoding the two peotein components of the enzyme," (1995) Cell, 81:677	
	BF	Conrad et al., "RAP1 protein interacts with yeast telomers in vivo: Overproduction alters telomere structure and decreases chromosome stability," (1990) Cell, 63:739	
	BG	Coombs, Dictionary of Biotechnology, Stockton Press, New York NY (1994)	
	вн	Cote et al., "Generation of human monoclonal antibodies reactive with cellular antigens," (1983) Proc. Natl. Acad. Sci., 80:2026	
	ВІ	Counter et al., "The catalytic subunit of yeast telomerase," (1997) Proc. Natl. Acad. Sci., 94:9202	
	ВЈ	Counter et al., (1994) Proc. Natl. Acad. Sci., 91:2900	
	вк	Creighton, Proteins, Structures and Molecular Principles, WH Freeman and Co, New York, NY (1983)	
	BL	Dieffenbach and Dveksler, PCR Primer, a Laboratory Manual, Cold Spring Harbor Press, Plainview NY (1995)	

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	ВМ	Duplaa et al., "Quantitative analysis of polymerase chain reaction products using biotinylated dUTP incorporation," (1993) Anal. Biochem., 212:229	
	BN	Fang <i>et al.</i> , "Oxytricha telomere-binding protein: separable DNA-binding and dimerization domains of the α-subunit," Genes Develop. 7:870 (1993) and Gray <i>et al.</i> , (1991) Cell 67:807	
	во	Feng et al., "The RNA Componant of Human Telomerase," (1995) Science, 269:1236	
	ВР	GenBank Accession No. AA281296	
	BQ	Genbank accession no. AA299878	
	BR	Genbank accession no. AA311750	
	BS	Gilley et al., "Altering specific telomerase RNA template residues affects active site function," (1995) Genes Develop., 9:2214	
	ВТ	Gottschling and Cech, "Chromatin Structure of the Molecular Ends of Oxytricha Mononuclear DNA: Phased Nucleosomes and a Telomeric Complex," (1984) Cell, 38:501	
	BU	Gottschling and Zakian, "Telomere proteins: specific recognition and protection of the natural termini of Oxytricha macronuclear DNA," (1986) Cell 47:195	
	BV	Grant et al., Meth Enzymol., (1987) 153:516-544	
	BW	Greenwood et al., "Phylogenetic relationships within the class oligohymenophorea, phylum ciliophora, inferred from the complete small subunit rRNA gene sequences of Colpidium campylum, Glaucoma chattoni, and Opisthonecta henneguyi," (1991) J. Mol. Evol., 3:163	
	вх	Greider and Blackburn, "A telomeric sequence in the RNA of Tetrahymena telomerase required for telomere repeat synthesis," (1989) <i>Nature</i> , 337:331	
	BY	Greider and Blackburn, "Identification of a specific telomere terminal transferase activity in Tetrahymena extracts," (1985) Cell, 43:405	

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Attorney Docket Number

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Signature	Considered	

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	CN	Koehler and Milstein, "Continuous cultures of fused cells secreting antibody of predefined specificity," (1975) Nature 256:495	
	со	Kosbor et al., "The production of monoclonal antibodies from human lymphocytes," (1983) Immunol. Today 4:72	
	СР	Lamond and Sproat, (1994)"Isolation and Characterization of Ribonucleoprotein Complexes," pp103-140	
	cq	Lamond et al., "Probing the structure and function of U2 snRNP with antisense oligonucleotides made of 2'-OMe RNA," (1989) Cell, 58:383	
	CR	Lendvay et al., "Senescence mutants of Saccharomyces cerevisiae with a defect in telomere replication identify three additional EST genes," (1996) Genetics, 144	
	cs	Lingler et al., "Purification of telomerase from Euplotes adeiculatus: requirement of a primer 3' overhang," (1996) Proc. Natl. Acad. Sci., 93:10712	
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	CU	Lingner et al., " Telomerase RNAs of different ciliates have a common secondary structure and a permuted template, " (1994) Genes Develop., 8:1984	
	CV	Lingner et al., "Telomerase and DNA End Replication: No Longer a Lagging Strand Problem?," (1995) Science 269:1533	
	cw	Lowy et al., "Isolation of transforming DNA: Cloning the hamster aprt gene," (1980) Cell, 22:817	
	сх	Lustig and Petes, Identification of yeast mutants with altered telomere structure," (1986) <i>Proc. Natl. Acad. Sci.</i> , 83:1398	
-	CY	Maddox et al., "Elevated serum levels in human pregnancy of a molecule immunochemically similar to eosinophil granule major basic protein," (1983) J. Exp. Med., 158:1211	
	cz	Makarov et al., "Nucleosomal Organization of Telomere-Specific Chromatin in Rat," (1993) Cell, 73:775	
	DA	McEachern and Blackburn, "runaway telomere elongation caused by telomerase RNA gene mutation," (1995) Nature, 376:403	

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·	DB	Melby et al., "Quantitative measurement of human cytokine gene expression by polymerase chain reaction," (1993) J. Immunol. Meth., 159:235	
	DC	Merrifield, "Solid phase peptide synthesis. I. The synthesis of a tetrapeptide," (1963) J. Am. Chem. Soc., 85:2149	
	DD	Meyerson et al., "hEST2, the Putative Human Telomerase Catalytic Subunit Gene, Is Up-Regulated in Tumor Cells and during Immortalization," (1997) Cell, 90:785	
	DE	Murray, In McGraw Hill Yearbook of Science and Technology, (1992) McGraw Hill, New York NY, pp 191-196	
	DF	Nakamura et al., "Telomerase Catalytic Subunit Homologs from Fission Yeast and Human," (1997) Science, 277:955	
	DG	Nakayama et al., "TLP1: A Gene Encoding a Protein Component of Mammalian Telomerase Is a Novel Member of WD Repeats Family," (1997) Cell,88:875	
	DH	Nielsen et al., (1993) "Peptide nucleic acids (PNAs): Potential antisense and anti-gene agents," Anticancer Drug Des., 8:53	
	Di	Oka et al., "Inverted terminal repeat sequence in the macronuclear DNA of Stylonychia pustulata, " (1980) Gene, 10:301	
	DJ	Olovnikov, "A theory of marginotomy: The incomplete copying of template margin in enzymic synthesis of polynucleotides and biological significance of the phenomenon," (1973) <i>J. Theor. Biol.</i> , 41:181	
	DK	Orlandi et al., "Cloning immunoglobulin variable domains for expression by the polymerase chain reaction," (1989) Proc. Natl. Acad. Sci., 86:3833	
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	DM	Price, (1993) Blood Rev., 7:127	
	DN	Rhodes et al., "Transformation of maize by electroporation of embryos," (1995) Meth. Mol. Biol., 55:121	
	DO	Roberge et al., "A strategy for a convergent synthesis of N-linked glycopeptides on a solid support," (1995) Science, 269:202	

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INFORMATION DISCLOSURE	Application Number	To Be Assigned
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STATEMENT BY APPLICANT	First Named Inventor	Cech, Thomas J.
	Group Art Unit	To Be Assigned
(use as many sheets as necessary)	Examiner Name	To Be Assigned
Sheet 9 of 10	Attorney Docket Number	015389-002630US

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
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	DP	Romero and Blackburn, "A conserved secondary structure for telomerase RNA, " (1991) Cell, 67:343	
	DQ	Sambrook et al., Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview NY (1989)	
	DR	Sandell et al., "Transcription of yeast telomere alleviates telomere position effect without affecting chromosome stability, "(1994) Proc. Natl. Acad. Sci., 91:12061	
	DS	Sanger et al., "DNA sequencing with chain-terminating inhibitors," (1977) Proc. Natl. Acad. Sci., 74:5463	
	DT	Scharf et al., "Heat stress promoters and transcription factors," (1994) Result Probl. Cell Differ. 20:125	
	DU	Shampay and Blackburn, "Generation of telomere-length heterogeneity in Saccharomyces cerevisiae," (1988) Proc. Natl. Acad. Sci., 85:534	
	DV	Sheen and Levis, "Transposition of the LINE-like retrotransposon TART to <i>Drosophila</i> chromosome termini," (1994) <i>Proc. Natl. Acad. Sci.</i> , 91:12510	
	DW	Singer and Gottschling, "TLC1: Template RNA Component of Saccharomyces cerevisiae Telomerase," (1994) Science 266:404	
	DX	Starling et al., "Extensive telomere repeat arrays in mouse are hypervariable," (1990) Nucleic Acids Res., 18:6881	
	DY	Swanton et al., "Arrangement of Coding and Non-coding Sequences in the DNA Molecules Coding for rRNAs in Oxytricha sp.," (1980) Chromosoma 77:203	
	DZ	Tommerup et al., "Unusual chromatin in human telomeres," (1994) Mol. Cell. Biol., 14:5777	
	EA	Trask, "Fluorescence in situ hybridization: application in cytogenetics and gene mapping," (1991) <i>Trends Genet.</i> , 7:149	
	EB	Verma et al., "Human Chromosomes: A Manual of Basic Techniques," Pergamon Press, New York NY (1988)	
	EC	Watson, "Origin of concatermeric T7 DNA, " (1972) Nature New Biol., 239:197	

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	ED	Weinrich et al., "Reconstitution of human telomerase with the template RNA component hTR and the catalytic protein subunit hTRT," (1997) Nat. Genet., 17(4):498	
	EE	Wellinger et al., "Origin activation and formation of single-strand TG _{1.3} tails occur sequentially in late S phase on a Yeast linear plasmid," (1993) <i>Mol. Cell. Biol.</i> , 13:4057	
	EF	Wellinger et al., "Saccharomyces Telomeres Acquire Single-Strand TG ₁₋₃ Tails Late in S Phase," (1993) Cell 72:51	
	EG	Whitehead Institute/MIT Center for Genome Research, Genetic Map of the Mouse, Database Release 10, APril 28, 1995	
	EH	Wigler et al., "Transfer of purified herpes virus thymidine kinase gene to cultured mouse cells," (1977) Cell, 11:223	
	EI	Wigler et al., "Transformation of mammalian cells with an amplifiable dominant-acting gene," (1980) Proc. Natl. Acad. Sci., 77:3567	
	EJ	Winter and Milstein, "Man-made antibodies," (1991) Nature, 349:293	
	EK	Wright et al., "Saccharomyces telomeres assume a non-nucleosomal chromatin structure, " (1992) Genes Develop., 6:197	
	EL	Yu et al., "In vivo alteration of telomere sequences and senescence caused by mutated Tetrahymena telomerase RNAs," (1990) Nature, 344:126	
	EM	Zahler and Prescott, "Telomere terminal transferase activity in the hypotrichous ciliate Oxytricha nova and a model for replication of the ends of linear DNA molecules," (1988) Nucleic Acids Res., 16:6953	
	EN	Zakian, Telomeres: Beginning to Understand the End," (1995) Science 270:1601	
	EO	Zaug et al., "Catalysis of RNA Cleavage by a Ribozyme Derived from the Group I Intron of Anabaena Pre-tRNA ^{Leu} ,"	

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